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Risk factors for pneumonia among patients with Parkinson's disease: a Taiwan nationwide population-based study

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Objective: Pneumonia is the leading cause of death in patients with Parkinson's disease (PD). However, few studies have been performed to explore the risk factors for pneumonia development in patients with PD.

Methods: We conducted a nationwide population-based cohort study of patients with PD to identify the risk factors for these patients developing pneumonia. Participants with newly diagnosed PD between 2000 and 2009 were enrolled from the 2000–2010 National Health Insurance Research Database in Taiwan. We compared patients with PD with an incidence of hospitalization with pneumonia vs those without, and Cox proportional hazard models were used to estimate the risk of pneumonia.

Results: Of the 2,001 enrolled patients (mean follow-up duration 5.8 years, range: 2.7–14.7 years), 381 (19.0%) had an incidence of hospitalization with pneumonia during the study period. Multivariate Cox proportional hazards analysis identified older age group (≥80 years of age, hazard ratio [HR] =3.15 [95% confidence interval 2.32–4.28]), male sex (HR =1.59 [1.29–1.96]), certain geographic regions (northern, HR =1.36 [1.04–1.78], southern and eastern, HR =1.40 [1.05–1.88]), rural areas (HR =1.34 [1.05–1.72]), chronic heart failure (HR =1.53 [1.02–2.29]), and chronic kidney disease (HR =1.39 [1.03–1.90]) as risk factors for hospitalization with pneumonia in patients with PD. However, treatment for dental caries was a protective factor (HR =0.80 [0.64–0.99]).

Conclusion: The results of this study highlight risk factors that are associated with hospitalization with pneumonia, and, for the first time, suggest a link between treated dental caries and a diminished risk of hospitalization with pneumonia in patients with PD.

Keywords: pneumonia, Parkinson's disease, dental caries, chronic heart failure, chronic kidney disease

Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder characterized by bradykinesia, rigidity, resting tremor, and postural instability.[1,2] With progression of the disease, the response to levodopa decreases and various problems that are less dopa responsive (or dopa resistant) develop, such as cognitive dysfunction and speech and swallowing problems.[3,4] Studies have documented a very high prevalence of oropharyngeal dysphagia in patients with PD,[5] which predisposes to aspiration pneumonia. Pneumonia in turn is a major reason for hospitalization of patients with PD and it is the leading cause of mortality in patients with PD (in one prospective study accounting for 64% of deaths).[6,7]

Pneumonia is a very common infectious disease and is one of the ten leading causes of death in the world.[8] Several risk factors for pneumonia in the general population,

including chronic pulmonary disease, chronic heart failure, diabetes, chronic liver disease, chronic kidney disease, cochlear implants, cerebrospinal fluid shunts, splenic dysfunction, and HIV/AIDS, have been recognized.[9–12] In PD, aspiration pneumonia is thought to be a multifactorial event, and aspiration alone is insufficient to cause pneumonia. Other important factors include alterations in the bacterial flora of the oropharynx, as well as impaired pulmonary clearance and host resistance. To our knowledge, however, there have been no population-based studies exploring the risk factors for pneumonia in patients with PD. Thus, we conducted a cohort study of patients with PD to identify the risk factors associated with pneumonia using a nationwide longitudinal population-based database.

Methods

Data source

Data for this study were derived from the 2000–2010 National Health Insurance Research Database (NHIRD), developed and managed by the Taiwan National Health Insurance Program for research purposes. The Taiwan National Health Insurance Program, since its introduction in 1995, has provided approximately 99% of Taiwan residents with comprehensive and universal health care.[13] We used one of the subsets of the NHIRD, composed of 1 million randomly selected subjects (constituting nearly 5% of the total Taiwan population) drawn in 2000. The NHIRD includes data on patients' demographic characteristics, diagnoses, and prescription claims (medication types, prescription dates, dosage, and duration supplied). The study was approved by the Institutional Review Board at Kaohsiung Medical University Hospital, and informed consent was waived by the Institutional Review Board because the data obtained from the NHIRD have been de-identified.

Design and study population

The PD cohort comprised patients who were newly diagnosed (between January 1, 2000 and December 31, 2009) based on the *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnostic criteria (ICD-9-CM code 332). Patients were diagnosed by neurologists and received antiparkinsonian medication(s) (levodopa and decarboxylase inhibitor, entacapone, bromocriptine, pergolide, cabergoline, ropinirole, pramipexole, amantadine, or selegiline) with at least three consecutive outpatient clinic visits, which were characterized as regular follow up.[14] Exclusion criteria were as follows: age <40 years; dementia, psychosis, or stroke before the diagnosis of PD (because of the potential for diagnostic confusion with dementia with Lewy bodies or vascular parkinsonism); and patients having a pneumonia-related diagnosis before PD diagnosis (Figure 1). We also identified patients with PD with dementia that occurred ≥1 year after the diagnosis of PD (termed PD dementia; ICD-9-CM codes 290, 294.1, 331.0).[1]

An incidence of hospitalization with pneumonia

Cases were determined by claims for hospital admissions using the following pneumonia-related codes: principal diagnosis of pneumonia (codes 480 to 487.0) or principal diagnosis of acute respiratory failure (code 518.81) or septicemia (code 038) with pneumonia as a secondary diagnosis.[15] All enrolled patients with PD were followed-up until one of the following events occurred: first-time pneumonia diagnosis, death, the end of follow-up in the medical records, or the end of 2010. The study flowchart is shown in Figure 1.

Risk factors related to pneumonia

We identified the inpatient and outpatient diagnosis files and prescription files of patients with PD before they were diagnosed with PD[16] to ascertain their history of diabetes mellitus, alcoholism, chronic pulmonary disease, dental caries, periodontitis, osteoporosis, chronic heart failure, chronic kidney disease, rheumatoid arthritis, chronic liver disease, cancer, epilepsy, asplenia after operation, cerebrospinal fluid shunt, multiple sclerosis, sickle cell disease, celiac disease, and HIV/AIDS, using ICD-9-CM codes and/or anatomical therapeutic chemical classification system codes.[9,14,17,18] Of note, we used the diagnosis of dental caries or periodontitis based on ICD-9-CM and anatomical therapeutic chemical codes and required at least three visits as a proxy for treated dental illness (Table S1).

Statistical analysis

The chi-square test and *t*-test were used to compare the demographic and clinical characteristics of patients with PD with, vs those without, pneumonia. The Kaplan–Meier method was used to estimate the probability of pneumonia. The Cox proportional hazards model was applied to analyze the effect of single and multiple covariates in predicting pneumonia development in patients with PD. All statistical analyses were performed with SAS Version 9.3 (SAS Institute, Cary, NC, USA). A P-value <0.05 was considered statistically significant.

Results

Demographic and clinical characteristics of the study population

After excluding subjects who did not meet the study criteria, a total of 2,001 patients with newly diagnosed

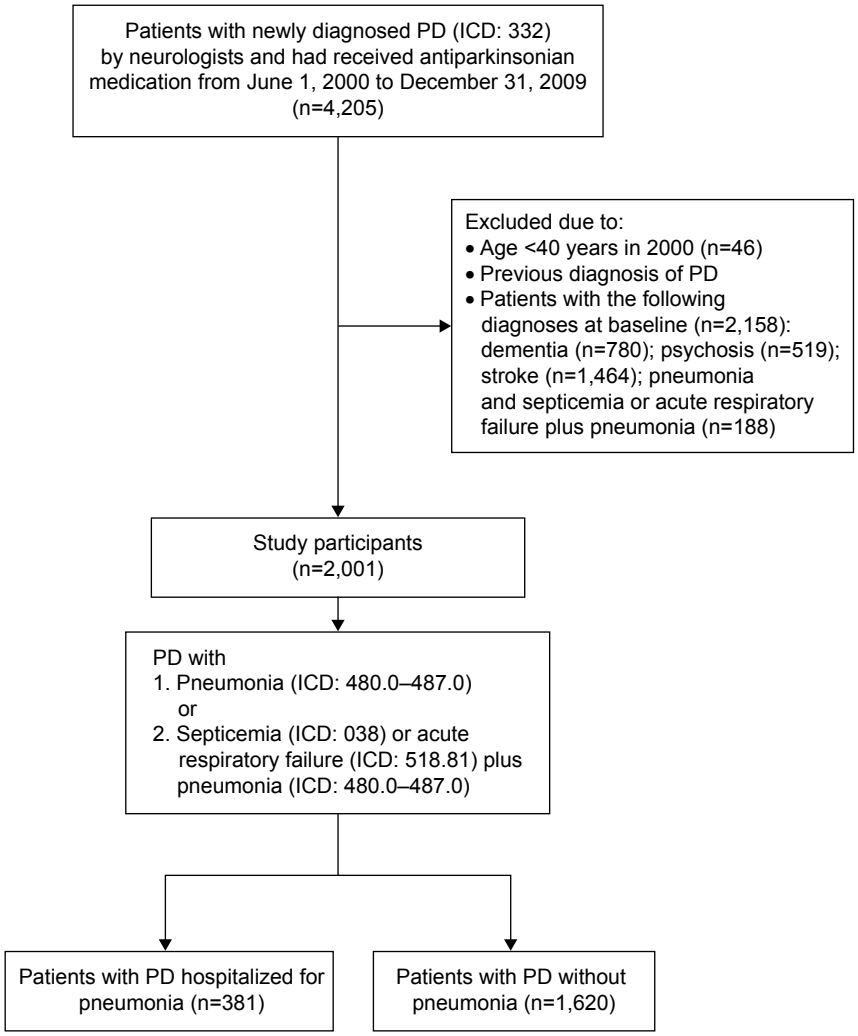

Figure 1 Flowchart of the study cohort assembly from medical records in Taiwan's National Health Insurance Research Database.
Abbreviations: PD, Parkinson's disease; ICD, International classification of disease.

PD were identified. The mean duration of follow-up was 5.77 years ± (standard deviation) 3.1 years. Of the 2,001 patients with PD, 381 (19.0%) had an incidence of hospitalization with pneumonia, with a mean latency after PD diagnosis of 4.3±2.6 years. Among the patients with PD in our study, several baseline characteristics were associated with the occurrence of pneumonia, including older age, male sex, geographic region of Taiwan (northern, southern, and eastern), lower income, fewer dental appointments, and also subsequent development of dementia (Table 1).

Comorbid physical conditions in enrolled patients with PD

After excluding dementia, psychosis, and stroke, the most common comorbid physical diseases were dental caries (48.1% of enrolled patients), periodontitis (44.1%), chronic pulmonary disease (37.4%), diabetes mellitus (25.6%), and chronic liver disease (19.7%) (Table 2). Comorbidities with a low incidence were cancer (n=42), epilepsy (n=29), asplenia after operation (n=4), cerebrospinal fluid shunt (n=3), and multiple sclerosis (n=3). There were no patients with sickle cell disease, celiac disease, or HIV/AIDS.

Risk factors for pneumonia in the PD cohort (univariate Cox proportional hazards analysis)

A univariate Cox proportional hazards analysis showed that patients with PD with chronic pulmonary disease, dental caries, chronic heart failure, and chronic kidney disease were at increased risk of developing pneumonia (Table 2). Multivariate Cox proportional hazards analysis identified the following as risk factors for pneumonia (Table 3): older age (70–79 years: hazard ratio [HR] =2.12, 95% confidence interval [CI] 1.64–2.75, $P<0.001$; ≥80 years: HR =3.15,

Table 1 Characteristics of patients with PD with and without pneumonia

Patient characteristics	Patients with PD with pneumonia (n=381)	Patients with PD without pneumonia (n=1,620)	*P*-value
Age at enrolment, mean (SD), years	74.78 (7.46)	70.16 (9.17)	<0.001
Age group, years, n (%)			<0.001
<70	90 (23.6)	719 (44.4)	
70–79	200 (52.5)	667 (41.2)	
≥80	91 (23.9)	234 (14.4)	
Sex, n (%)			<0.001
Male	231 (60.6)	782 (48.3)	
Female	150 (39.4)	838 (51.7)	
Geographic region of Taiwan, n (%)			0.015
Central	78 (20.5)	448 (27.7)	
Northern	188 (49.3)	713 (44.0)	
Southern and Eastern	115 (30.2)	459 (28.3)	
Urban level, n (%)			0.098
Urban and suburban	276 (72.4)	1,103 (68.1)	
Rural	105 (27.6)	517 (31.9)	
Monthly income, NT$, n (%)			<0.001
≥30,000	18 (4.7)	195 (12.0)	
<30,000	363 (95.3)	1,425 (88.0)	
Dental attendance rate, n (%)			<0.001
No	210 (54.3)	696 (42.9)	
Yes	177 (45.7)	927 (57.1)	
PD with dementia,[a] n (%)	102 (26.4)	264 (16.3)	<0.001

Note: [a]Dementia occurred at least 1 year after diagnosis of PD.
Abbreviations: PD, Parkinson disease; SD, standard deviation; NT$, new Taiwan dollar.

95% CI 2.32–4.28, $P<0.001$); male sex (HR =1.59, 95% CI 1.29–1.96, $P<0.001$); geographic region of Taiwan (northern: HR =1.36, 95% CI 1.04–1.78, $P=0.024$; southern and eastern: HR =1.40, 95% CI 1.05–1.88, $P=0.023$); rural areas (HR =1.34, 95% CI 1.05–1.72, $P=0.021$); chronic heart failure (HR =1.53, 95% CI 1.02–2.29, $P=0.042$); and chronic kidney disease (HR =1.39, 95% CI 1.03–1.90, $P=0.034$). However, treatment for dental caries was a protective factor (HR =0.80, 95% CI 0.64–0.99, $P=0.036$). Figure 2 shows the Kaplan–Meier analysis of the incidence of pneumonia in male and female patients with PD. Based on the analysis, we found similar patterns of pneumonia incidence in the male and female groups in the first 2 years after PD diagnosis; however, pneumonia incidence increased more rapidly in the male group during the follow-up period.

Discussion

To the best of our knowledge, this is the first study to identify risk factors for pneumonia in the PD population. This study used a nationwide population-based screening

Table 2 Comorbidities and risk of pneumonia – univariate Cox proportional hazards analysis

Comorbidities, n (%)	Patients with PD with pneumonia (n=381)	Patients with PD without pneumonia (n=1,620)	*P*-value	Crude HR	(95% CI)	*P*-value	Adjusted HR	(95% CI)[a]	*P*-value
Diabetes mellitus	90 (23.6)	423 (26.1)	0.317	1.20	(0.95–1.53)	0.125	1.10	(0.86–1.40)	0.438
Alcoholism	37 (9.7)	150 (9.3)	0.785	1.35	(0.96–1.89)	0.087	1.24	(0.88–1.75)	0.229
Chronic pulmonary disease	145 (38.3)	603 (37.2)	0.690	1.41	(1.14–1.73)	0.001	1.14	(0.92–1.41)	0.231
Dental caries	141 (37.0)	822 (50.7)	<0.001	0.76	(0.61–0.93)	0.008	0.80	(0.64–0.99)	0.036
Periodontitis	134 (35.2)	748 (46.2)	<0.001	0.83	(0.67–1.02)	0.077	0.89	(0.69–1.14)	0.339
Osteoporosis	63 (16.5)	321 (19.8)	0.144	1.10	(0.84–1.44)	0.499	1.12	(0.84–1.49)	0.430
Chronic heart failure	26 (3.8)	75 (4.6)	0.078	1.95	(1.31–2.91)	0.001	1.53	(1.02–2.29)	0.042
Chronic kidney disease	48 (12.6)	180 (11.1)	0.411	1.60	(1.18–2.17)	0.002	1.39	(1.03–1.90)	0.034
Rheumatoid arthritis	18 (4.7)	72 (4.4)	0.812	1.31	(0.82–2.11)	0.260	1.26	(0.78–2.04)	0.339
Chronic liver disease	51 (13.4)	343 (21.2)	0.001	0.83	(0.62–1.12)	0.215	0.77	(0.57–1.05)	0.100

Notes: [a]Adjusted for age group, sex, geographic region, level of urbanization, monthly income, PD with dementia, and comorbidities including chronic pulmonary disease, dental caries, chronic heart failure, and chronic kidney disease.
Abbreviations: PD, Parkinson's disease; HR, hazard ratio; CI, confidence interval.

Table 3 Risk factors for pneumonia – multivariate Cox proportional hazards analysis

Risk factors	Adjusted HR	(95% CI)	*P*-value	Female (n=988)			Male (n=1,022)		
				Adjusted HR	(95% CI)	*P*-value	Adjusted HR	(95% CI)	*P*-value
Age group, years									
<70	1.00	–	–	1.00	–	–	1.00	–	–
70–79	2.12	(1.64–2.75)	<0.001	2.69	(1.78–4.05)	<0.001	1.80	(1.28–2.52)	0.001
≥80	3.15	(2.32–4.28)	<0.001	4.18	(2.56–6.84)	<0.001	2.57	(1.74–3.81)	<0.001
Sex									
Female	1.00	–	–	–	–	–	–	–	–
Male	1.59	(1.29–1.96)	<0.001	–	–	–	–	–	–
Geographic region of Taiwan									
Central	1.00	–	–	1.00	–	–	1.00	–	–
Northern	1.36	(1.04–1.78)	0.024	1.42	(0.90–2.24)	0.135	1.33	(0.95–1.86)	0.096
Southern and Eastern	1.40	(1.05–1.88)	0.023	1.49	(0.92–2.43)	0.105	1.34	(0.92–1.93)	0.126
Urban level									
Urban and suburban	1.00	–	–	1.00	–	–	1.00	–	–
Rural	1.34	(1.05–1.72)	0.021	1.43	(0.96–2.14)	0.078	1.33	(0.96–1.85)	0.083
Monthly income, NT$									
≥30,000	1.00	–	–	1.00	–	–	1.00	–	–
<30,000	1.50	(0.91–2.46)	0.114	1.83	(0.45–7.52)	0.400	1.57	(0.91–2.71)	0.108
PD with dementia[a]									
No	1.00	–	–	1.00	–	–	1.00	–	–
Yes	1.39	(0.92–2.10)	0.114	1.51	(0.73–3.12)	0.264	1.31	(0.79–2.17)	0.290
Comorbidities									
Chronic pulmonary disease	1.14	(0.92–1.41)	0.231	1.20	(0.84–1.71)	0.313	1.15	(0.88–1.52)	0.307
Dental caries	0.80	(0.64–0.99)	0.036	0.90	(0.64–1.27)	0.548	0.74	(0.56–0.97)	0.029
Chronic heart failure	1.53	(1.02–2.29)	0.042	2.22	(1.23–2.98)	0.008	1.14	(0.64–2.03)	0.649
Chronic kidney disease	1.39	(1.03–1.90)	0.034	1.03	(0.58–1.80)	0.931	1.65	(1.13–2.39)	0.009

Note: [a]Dementia occurred at least 1 year after diagnosis of PD.
Abbreviations: PD, Parkinson's disease; HR, hazard ratio; CI, confidence interval; NT$, new Taiwan dollar.

of patients with PD to estimate the risk of hospitalization with pneumonia in Taiwan. A total of 2,001 patients with new-onset PD between 2000 and 2010 were identified in our cohort analysis. Overall, our study found that older age, male sex, geographic region of Taiwan, rural areas, chronic heart failure, and chronic kidney disease were independent risk factors for pneumonia among patients with PD. However, treatment for dental caries was a protective factor.

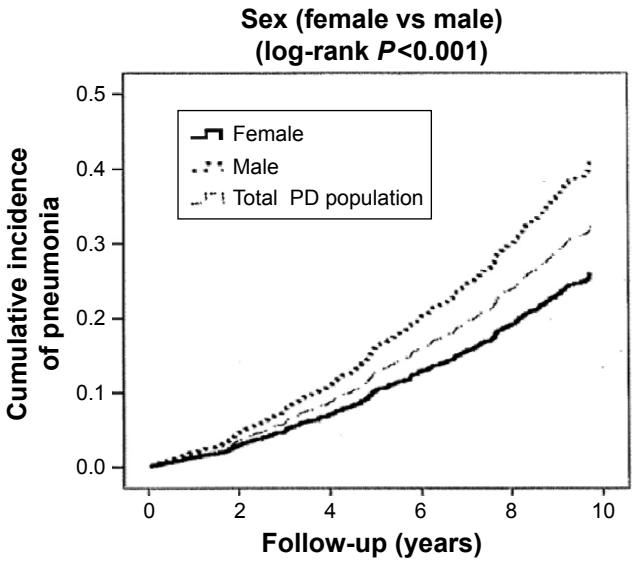

Figure 2 Kaplan–Meier analysis for incidence of pneumonia in patients with PD by sex.
Abbreviation: PD, Parkinson's disease.

In general, the incidence of pneumonia in the general population increases with age,[18–21] and is higher in males than in females.[9,20] The demographics of our PD population in terms of age and sex were similar to those of the general population in these studies. Male patients with PD had a higher risk (HR =1.59) of developing pneumonia (after adjusting for other confounding factors) than female patients. Although male vulnerability to pneumonia has long been recognized, and the consistency and magnitude of these differences between the sexes are particularly impressive in patients with interstitial pneumonia or ventilator-associated pneumonia,[22,23] the underlying mechanisms responsible for this phenomenon are still unclear. Our study found that the incidence of pneumonia among patients with PD was lower in central Taiwan and urbanized/suburbanized regions. The results suggest that environmental factors may play a role in pneumonia risk in the PD population, and one possible reason may be a relative lack of access to health care resources. There is some literature reporting geographic differences in pneumonia incidence

in the pediatric population, but this has not previously been observed in the PD population.[21,24]

Our study showed that chronic heart failure and chronic kidney disease are both independent predictive factors for pneumonia in patients with PD. Of all the comorbidities in this study, chronic heart failure had the largest magnitude as a risk factor for pneumonia (HR =1.53) (and particularly in females aged >80 years old – Table S2), which is comparable to the twofold increased risk of pneumonia in the general population.[25,26] Chronic kidney disease was associated with an increased risk of pneumonia among patients with PD in our study, similar to that in the general population, and this risk was particularly seen in older male patients.[11,20] Although chronic pulmonary disease is recognized as an important risk factor for pneumonia in the general population,[20] for reasons that are unclear, this did not emerge as a risk factor in our study.

Of interest, we found that patients with PD who had received treatment for dental caries suffered less from pneumonia (especially in males aged <70 years old) (Table S3). Poor oral health, including dental caries and periodontal diseases, is commonly observed in patients with PD, even in the early stages of the disease.[27–29] The high prevalence of impaired swallowing, periodontal diseases, and caries may lead to a greater risk of aspiration pneumonia.[30–33] Maintenance of good oral hygiene and control of oral biofilm formation in the elderly reduce the number of potential respiratory pathogens in the oral secretions, which in turn reduces the risk of pneumonia.[34] Our findings suggest that patients with PD who received treatment for dental caries may have better oral health and a reduced risk of pneumonia than those who did not. Although we cannot determine based on the available data whether there were differences in dysphagia between the two groups, we believe our results highlight the potential importance of good oral health in reducing morbidity and mortality in patients with PD. In brief, patients with PD had similar risk factors for pneumonia hospitalization when compared to general population. Our study found that chronic heart failure, chronic kidney disease, and dental caries were more significant risk factors for pneumonia hospitalization among patients with PD.

The main strength of our study is that it provides information from a nationwide population-based cohort with a large sample size, and the results may provide a good representation of ethnic Chinese patients with PD. To increase the accuracy of the diagnosis of PD, the study population was obtained by linking an ambulatory care expenditures database (neurologists and ICD-9-CM code) and a prescription claims database (medical treatment for PD). Moreover, covariates, including common underlying diseases (especially dental illness), were taken into consideration. Nevertheless, there are some limitations in our study that deserve comment. First, the study was retrospective. We did not have the opportunity to review all the medical charts of patients from the de-identified National Institutes of Health database. Second, although we analyzed national health care records from a database of 1 million randomly selected subjects, there were still relatively few PD cases to allow us to make a more precise estimation of total PD populations in Taiwan. Third, information on other risk factors contributing to pneumonia, such as the severity of comorbidities, lifestyle factors, such as smoking and alcohol consumption, and biochemistry data were unavailable for retrieval from the database. Other lifestyle-related pneumonia risk factors, including contact with children and nutritional status, were not included in the study. Finally, it was difficult to distinguish between aspiration pneumonia and infectious pneumonia from the details available in the database.

Conclusion

Identification of risk factors for hospitalization with pneumonia among patients with PD in Taiwan has highlighted chronic heart failure, chronic kidney disease, and oral hygiene as being associated with an increased risk of pneumonia. In particular, older female patients with PD with chronic heart failure and older male patients with PD with chronic kidney disease had a significantly higher risk of pneumonia. In contrast, male patients with PD had a diminished risk of pneumonia if dental caries were treated previously. Early recognition and prompt management of comorbid physical diseases/risk factors in patients with PD may help to reduce the risk of hospitalization with pneumonia, and thus, the burden of the disease.

Acknowledgments

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Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Table S1 ICD-9-CM codes and ATC classification system codes used in this study

Main diseases	ICD-9-CM codes
Parkinson disease	332
Dementia	290, 294.1, 331.0
Stroke	430–434, 436–438
Psychoses	295, 297
Pneumonia	480.0, 487.0
Septicemia	038
Acute respiratory failure	518.81
Comorbidities	**ICD-9-CM codes and ATC codes**
Diabetes mellitus	249.XX–250.XX, 648.01, 648.02, 588.1, 357.2
Alcoholism	291.XX, 303.0X, 303.9, 305.00–305.02, 571.0–571.5, 571.8–571.9, 980.0, 980.2, 980.3, 980.8, 980.9, 977.3, V11.3
Chronic pulmonary disease	416.8, 416.9, 490, 491–495, 496, 500–505, 506.4, 508.1
Dental caries	521.0, 521.1, 521.2, 521.3, 522.0, 522.1, 522.2, 522.3, 522.4, 522.5, 522.6, 522.7, 522.8, 522.9; 89001C–89005C, 89008C–89012C, 89101C–89105C, 89108C–89112C, 89006C, 90004C, 90005C, 90013C, 90014C, 90015C, 90016C, 90017C, 92013C, 92014C, 92015C, 92016C, 92055C
Periodontitis	523.0, 523.1, 523.2, 523.3, 523.4, 523.5, 523.8, 523.9; 91001C, 91003C, 91004C, 91006C–91008C, 91104C, P4001C, P40002C, 91009B, 91010B, 92027C, 92033C, 92071C, 91011C, 91012C, 91013C, 92013C, 92014C, 92015C, 92016C, 92055C
Osteoporosis	733.0X
Chronic heart failure	402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4, 425.9, 428.4X
Chronic kidney disease	581–583, 585–587
Rheumatoid arthritis	714.0, 714.1, 714.2, 714.30–714.33, 714.4
Chronic liver disease	571.40, 571.41, 571.49, 571.2, 571.5, 571.6, 572.2
Cancers	140–208
Epilepsy	345.XX, 649.40–649.44, 780.3
Asplenia after operation	414.2, 414.3, 415
Cerebrospinal fluid shunt	83049B
Multiple sclerosis	340
Sickle cell or coeliac disease	282.60
HIV/AIDS	042, 079.53, 795.71
Drug categories	**ATC codes**
Levodopa	N04BA01
Levodopa and decarboxylase inhibitor	N04BA02
Levodopa, decarboxylase inhibitor, and COMT inhibitor	N04BA03
Entacapone	N04BX02
Bromocriptine mesylate	N04BC01
Pergolide mesylate	N04BC02
Cabergoline	N04BC06
Ropinirole	N04BC04
Pramipexole	N04BC05
Amantadine	N04BB01
Selegiline	N04BD01

Abbreviations: ICD-9-CM, International Classification of Disease, Ninth Revision, Clinical Modification; ATC, anatomical therapeutic chemical.

Table S2 Adjusted hazard ratio for pneumonia in the study population with PD stratified by age group and sex

Variables	<70 years old group					70–79 years old group					≥80 years old group				
	No cases	(%)	Adjusted HR	(95% CI)	*P*-value	No cases	(%)	Adjusted HR	(95% CI)	*P*-value	No cases	(%)	Adjusted HR	(95% CI)	*P*-value
Male			n=384					n=437					n=192		
Chronic pulmonary disease	17	(15.3)	1.36	(0.76–2.44)	0.306	50	(25.6)	1.23	(0.84–1.80)	0.292	30	(27.3)	0.81	(0.46–1.40)	0.447
Dental caries	16	(8.4)	0.49	(0.27–0.92)	0.027	44	(21.2)	0.71	(0.49–1.05)	0.086	25	(28.7)	1.03	(0.57–1.86)	0.932
Chronic heart failure	2	(22.2)	1.77	(0.41–7.66)	0.447	5	(17.2)	0.89	(0.35–2.22)	0.796	6	(42.9)	1.79	(0.73–4.39)	0.203
Chronic kidney disease	4	(14.3)	1.34	(0.46–3.91)	0.594	16	(28.1)	1.34	(0.78–2.31)	0.290	14	(43.8)	2.23	(1.14–4.35)	0.019
Female			n=425					n=430					n=133		
Chronic pulmonary disease	10	(8.4)	1.70	(0.79–3.66)	0.179	29	(17.3)	1.05	(0.60–1.65)	0.845	10	(21.7)	1.26	(0.55–2.87)	0.586
Dental caries	13	(5.5)	0.79	(0.38–1.66)	0.537	30	(16.3)	0.91	(0.28–1.45)	0.703	13	(23.2)	1.12	(0.54–2.31)	0.757
Chronic heart failure	1	(6.7)	0.73	(0.09–5.96)	0.768	6	(24.0)	1.72	(0.73–4.06)	0.218	6	(66.7)	4.81	(1.74–13.32)	0.003
Chronic kidney disease	2	(5.3)	0.88	(0.20–3.92)	0.864	11	(18.0)	1.23	(0.64–2.36)	0.533	1	(8.3)	0.52	(0.07–4.14)	0.538

Notes: Adjusted age group, sex, geographic region of Taiwan, urban level, monthly income, severity of physical condition, PD with dementia, and comorbidities, including chronic pulmonary disease, dental caries, chronic heart failure, and chronic kidney disease.
Abbreviations: PD, Parkinson's disease; HR, hazard ratio; CI, confidence interval.

Table S3 Adjusted hazard ratio for pneumonia in the study population with PD stratified by follow-up duration and sex

Variable	Overall				Female				Male			
	<2 years		≥2 years		<2 years		≥2 years		<2 years		≥2 years	
	Adjusted HR	(95% CI)	Adjusted HR	(95% CI)	Adjusted HR	(95% CI)	Adjusted HR	(95% CI)	Adjusted HR	(95% CI)	Adjusted HR	(95% CI)
Dental caries	0.58	(0.37–0.89)	0.76	(0.59–0.97)	0.39	(0.16–0.90)	1.00	(0.69–1.45)	0.76	(0.44–1.32)	0.62	(0.45–0.86)
Chronic heart failure	1.80	(0.87–3.75)	1.35	(0.80–2.25)	5.56	(0.97–31.83)	2.56	(1.34–4.87)	1.79	(0.77–4.16)	0.64	(0.26–1.57)
Chronic kidney disease	0.87	(0.48–1.57)	1.32	(0.91–1.92)	0.47	(0.15–1.51)	0.96	(0.49–1.87)	1.01	(0.49–2.10)	1.61	(1.02–2.56)

Notes: Adjusted age group, sex, geographic region of Taiwan, urban level, monthly income, severity of physical condition, PD with dementia, and comorbidities, including chronic pulmonary disease, dental caries, chronic heart failure and chronic kidney disease.
Abbreviation: PD, Parkinson's disease.